REMARKS

Applicant respectfully requests reconsideration. Claims 1-2, 4-7, 17, 18 and 101 were previously pending in this application. No claims have been canceled, added or amended. As a result, claims 1-2, 4-7, 17, 18 and 101 are pending for examination with claim 1 being the sole independent claim. No new matter has been added.

Claim Rejections under 35 U.S.C. §112, first paragraph – Enablement

Claims 1-2, 4-7, 17-18 and 101 are rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the enablement requirement. According to the Examiner, the specification does not enable one skilled in the art to practice the invention without an undue amount of experimentation. Applicant respectfully traverses. A person of ordinary skill in the art would not have to engage in undue experimentation to practice the claimed invention and the claimed invention was therefore enabled at the time of filing.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 Fed. Circ. 1988), and include (1) the breadth of the claims, (2) the nature of the invention, (3) the quantization of experimentation necessary, (4) the amount of direction or guidance presented, (5) the presence or absence of working examples, (6) the state of the prior art, (7) the relative skill of those in the art, and (8) the predictability of the art. Applicant will analyze the claimed invention according to the *Wands* factors and show that the claimed invention was enabled.

(1) Breadth of the claims /(2) nature of the invention

The claimed invention pertains to a method for treating an allergic condition other than asthma or eczema by the administration of a polymer with a specific charge motif. Firstly, the specification provides a genus of well characterized polymers with a specific charge motif and shows that the charge motif has the claimed functionality, namely the ability to treat allergic conditions. Secondly, the methods of treatment are directed to allergic conditions, which is a single category disease that is well described in the art. Thus, the specification in combination with the art provides support for the breath of the claims.

(3) the quantization of experimentation necessary / (4) the amount of direction or guidance presented.

The specification provides guidance, including working examples, on how to practice the methods of the claimed invention. The specification teaches how to treat an allergic condition by administering the polymers with the recited charge motif. In addition, the specification provides methods for evaluating the efficacy of the claimed treatment methods (*e.g.*, by measuring the suppression of the level of IgE antibodies).

(5) the presence or absence of working examples.

The specification provides working examples for the methods of the claimed invention. The specification teaches that polymers as diverse as peptides and polysaccharides show an immunomodulatory effect, as long as the polymers have the recited charge motif (See *e.g.*, Example 1, page 49 and Examples 6 and 7, pages 54-55). In addition, Examples 5 and 8 show that administration of the polymers with the recited charge motif results in a decrease in the level of IgE antibodies, which is all that is needed to show treatment of an allergic condition.

(6) the state of the prior art, (7) the relative skill of those in the art, and (8) the predictability of the art.

Allergic conditions are well described in the art. The art provides the pathophysiology and underlying biochemical mechanisms of allergic conditions (*i.e.*, the induction of a Th2 response by allergens resulting in the production of IgE and the subsequent activation of mast cells and basophilic cells, ultimately resulting in the toxic mediators that cause the allergic response) and treatment methods for allergic conditions (*e.g.*, glucocorticoids, antihistamines, beta-adrenergic agonists, anticholinergics, cytokines and anti-IgE antibodies). The art teaches that, because all allergic conditions operate through a similar underlying mechanism, treatment methods for allergic conditions often work on more than one allergic condition. Because the field of the treatment of allergic conditions is well established the predictability in the field is high.

Thus, based on the teachings in the specification and the state and predictability of the prior art, Applicant has met the burden of demonstrating that the claimed invention meets the enablement requirement as set forth *In re Wands*.

According to the Examiner, the genus of compounds encompassed by the instant claim recitation is nearly limitless, so it is unlikely that the genus of compounds could be well characterized. Respectfully, Applicant disagrees with this assertion.

Firstly, the size of genus of compounds has no relation to the characterization of these compounds. The specification provides that polymers as diverse as peptides and polysaccharides have a consistent immunomodulatory effect, as long as the polymers have the recited charge motif (See *e.g.*, Example 1, page 49 and Examples 6 and 7, pages 54-55). Furthermore, the specification has incorporated by reference US 5,679,654, US 5,700,787 and WO 00/59515. These documents provide a detailed analysis of polymers, including polysaccharides, with specific charge motifs and their immunomodulatory effects. The teachings in these documents show that polymers with the motif recited in the instant application have a predictable and consistent immunomodulatory effect, while polymers with a slightly different charge motif do not have such an effect (See *e.g.*, WO 00/59515, pages 35-43). Applicant notes that the Examiner acknowledges that some compounds of the genus are well characterized. Respectfully, Applicant believes that that characterization is not limited to "some compounds of the genus" as the specification clearly characterizes all compounds of the genus, as demonstrated above.

Secondly, the class of compounds with the recited polysaccharide charge motif is not "nearly limitless". For instance, Mazmanian et al., (cited by the Examiner in the Office Action) discuss the characteristics of polysaccharides PSA and PSB, which are examples of the polymers used in the methods of the claimed invention, and state "these molecules have an unprecedented structure: each molecule has both positively and negatively charged motifs in each repeating unit. It is unusual for a bacterial polysaccharides to be shown to have any positive charges, most are either neutral or negatively charged. It was proposed that this unique structural feature might be crucial for the T-cell activating property of PSA. This idea was eventually shown to be correct for both PSA and PSB" (Top right column page 852). Thus, polymers with the recited charge motif itself, as found in nature, are relatively unusual. The class of polymers with these charge motifs, including natural polysaccharides, is well defined and not "nearly limitless"

Further, according to the Examiner, the genus of allergic diseases exhibits diverse etiologies and phenotypes and the Examiner reasons that a treatment for one allergic disease therefore will not

be a treatment for all. Applicant respectfully disagrees with this statement. The pathophysiology and underlying biochemical mechanisms of allergic conditions, including allergic asthma, are well described and are the same for all allergic conditions. Allergic conditions are induced by a Th2 response to an allergen, characterized the production of Th2 cytokines such as IL4 and IL13, and resulting in the induction of IgE. In turn, IgE activates basophilic and mast cells resulting in the inflammatory and toxic mediators that cause the allergic reaction. While there may be minor variations in the mechanism of the various allergic disorders, the overall pathophysiology is the same. The art provides that anti-allergic therapies can be used for the treatment of more than one allergic disorder. For instance, an anti-IgE antibody (Omalizumab) has been used to treat a variety of allergic disorders, including uticaria, asthma and peanut anaphylaxis (See *e.g.*, Miller et al., Clinical and Molecular Allergy 2008, 6:4; provided herewith). Thus, a method of treatment that results in the lowering of the levels of IgE., such as the administration of an anti-IgE antibody, provides a method of treatment for multiple allergic condition. The specification provides working examples for the treatment of asthma with the polymers PSA1 and CP1, whereby the administration of the polymers results in the lowering of the levels of anti-allergen IgE antibodies. Because the lowering of IgE levels is a general method for the treatment of any allergic conditions, the specification enables the treatment of any allergic condition.

The Examiner argues that a treatment regimen that results in the lowering of allergen specific IgE levels is not an effective treatment method for the allergic condition (page 7). Respectfully, Applicant believes that this assertion is unreasonable as the art shows that the lowering of IgE levels is a method for the treatment of allergic disorders (See *e.g.*, Miller et al., Clinical and Molecular Allergy 2008, 6:4; provided herewith). In addition, Applicant believes that the Examiner has not met her burden in establishing a *prima facie* rejection in this matter because the Examiner provides no support for the statement that lowering the levels of IgE is not a method for the treatment of allergic disorders.

The Examiner states that Mazmanian et al. do not teach or suggest that zwitterionic polymers may be used to treat any particular allergy, much less all allergies, or that zwitterionic polymers have any direct effect on IgE production. The Examiner continues by stating that she is confused as to why Applicant is implying that zwitterionic polymers work to lower IgE levels.

Respectfully, Applicant does not understand the Examiner's confusion. The specification *shows* that the administration of the zwitterionic polysaccharides PSA and CP1 results in the lowering the levels of allergen induced IgE (Examples 5 and 8). Thus, Applicant provides a direct showing of the suppression of IgE levels by the administration of polymers with the recited charge motif. This direct showing can not be refuted by the Examiner's citation of a reference that, allegedly, is silent on the effects of IgE production. Furthermore, in contrast to the interpretation of the reference by the Examiner, Applicant believes that Mazmanian et al. support the claimed invention, at least because the reference teaches that correcting the Th2 bias by *B. fragilis* polysaccharides, which are examples of the polymers of the claimed invention, may lead to the suppression of the onset of allergic and asthmatic disorders.

The Examiner states on page 8 of the Office action that she "has *provided evidence* that the recited polymers are not predicted to work on all allergic diseases". Applicants respectfully disagree with the statement by the Examiner. Applicant believes that, at most, the Examiner has provided some general statements that zwitterionic polymers can affect the immune system in a variety of ways. However, the Examiner has not shown that the polymers of the claimed invention are not predicted to lower IgE levels and that that the lowering of IgE levels is not a method for treating allergic conditions. Respectfully, Applicant believes that the Examiner has not made out a *prima facie* case in this respect.

The Examiner referred to Kalka-Moll et al. to support the statement that different zwitterionic polymers have different cell stimulatory effects. Respectfully, Applicant maintains that the Examiner has misinterpreted the teachings of Kalka-Moll et al. Kalka-Moll et al. merely show that the immunomodulatory potency of the zwitterionic polysaccharides is dependent on the length of the polysaccharides. The teachings of Kalka-Moll et al. do not support the assertion that zwitterionic polymers having different structures stimulate cellular immunity differently as Kalka-Moll et al. do not teach that polysaccharides with the recited charge motifs have different immunomodulatory effects. Kalka-Moll et al. merely show that some polymers with the recited charge motif are more effective than others, which does not question the enablement of the claimed invention As stated in the MPEP (§2164.01) "The test of enablement is not whether any

experimentation is necessary, but rather whether, if experimentation is necessary, it is undue." *In re Angstadt*, 537 F.2d 498, 504.

According to the Examiner, "the term "comprising" is open language that opens the claimed polymers to include additional molecules wherein the methods are not the result of the charge motif of the polymers at all". Respectfully, Applicant maintains that the Examiner's interpretation of claims reciting the connector "comprising" has no legal basis. Firstly, Applicant has shown that the recited charge motif conveys the claimed functionality and that removal of the charge motif results in the loss of the claimed functionality. Thus, the polymers do not need to include "additional molecules" to obtain the claimed functionality. Secondly, the Examiner's assertion seems to challenge the use of the connector "comprising" in claim language in general. If the Examiner's argument were correct, no claim with the term "comprising" would be enabled because the claim could be interpreted to include additional components or steps that are required to obtain the claimed functionality.

The Examiner states on page 9 of the Office Action that she is confused as to why patients without infection, surgery and trauma, as recited in claim 4, are included in the methods of the claimed invention. Respectfully, Applicant has shown that the claimed invention is enabled for the any subject. The claimed invention, therefore, is also enabled for subjects without infection, surgery and trauma, as recited in claim 4

Thus, based on a *Wands* factor analysis, Applicant believes that Applicant has shown that claimed invention is enabled as no undue experimentation is required to practice the claimed invention. In addition, Applicant believes that the Examiner has not shown that the claimed invention does not meet the enablement requirements.

Claim Rejections under 35 U.S.C. §112, first paragraph – Written Description

Claims 1-2, 4-7, 17-18, and 101 are rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. According to the Examiner, the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time of filing, had

possession of the claimed invention. Further, according to the Examiner, Applicant is in possession of treating asthma in a mouse by injecting the mouse with isolated PSA1.

Applicant respectfully traverses. Based on the teachings in the specification, a person of ordinary skill in the art would understand that Applicant had possession of the claimed invention at the time of filing of the application.

The claimed invention pertains to a treatment of an allergic condition other than asthma or eczema by administration of a polymer with the recited charge motif. Applicant has shown that correlation exists between the structure of the recited polymers and the function of the claimed methods of treatment. Firstly, the specification provides a genus of well characterized polymers with a specific charge motif. Secondly, the specification shows that polymers as diverse as peptides and polysaccharides show an immunomodulatory effect, as long as they have the recited charge motif (See *e.g.*, Example 1, page 49 and Examples 6 and 7, pages 54-55). Thirdly, the methods of treatment are directed to allergic conditions, which is a single category disease that is well described in the art and is characterized by an increase in serum IgE in the subject. Fourthly, in Examples 5 and 8 of the specification (pages 52-57), Applicant shows that administration of the polymers with the recited charge motif result in a decrease in the level of IgE antibodies. Finally, the findings in the instant application are corroborated in the art, which has established the relationship between specific charge motif of the polymer and the immunomodulatory effect of the polymer. No more is required to show possession of the claimed invention.

According to the Examiner, the specification does not disclose a correlation structure of the polymer and function (ability to treat an allergic condition other than asthma) and in this case functional limitations (comprising repeating units of a charge motif characteristic of PSA) such that a skilled artisan would have known what polymers have the claimed function and functional limitations. The Examiner refers to *In re Kubin* and quotes "Without a correlation between structure and function, the claim does little more than define the claimed invention by function." Applicant respectfully disagrees with the assertion that the specification does not provide a correlation between structure and function. The specification provides what the structural requirements are for the polymers to have the claimed functionality. Namely, the polymer needs to have a structure comprising a repeating unit having a positively charged free amino moiety and a

negatively charged moiety. In addition, Applicant shows that if this charge motif is modified, the polymer looses its immunomodulatory capacity. Thus, a correlation between structure and function is provided and the claimed invention can be distinguished over the scenario presented in the *In re Kubin* citation.

The Examiner states that "the art shows that not all polymers encompassed by the instant claim recitations are able to stimulate cellular immunity." Respectfully, Applicant does not believe that the Examiner has made such a showing. Applicant has demonstrated above, that the art cited by the Examiner, Mazmanian et al. and Kalka-Moll et al., support the methods of the claimed invention and do not support the assertion that the polymers encompassed by the claimed invention are not able to stimulate cellular immunity.

Further, according to the Examiner, the "specification must also set forth the structural features that allow one of ordinary skill in the art to produce the genus of polymers comprising repeating units of a charge motif characteristic of PSA" and that "the instant application identifies PSA1 and CP1 that have properties called for in the instant claims, but there is no guidance on other polymers with these properties." Respectfully, the specification provides how to produce the polymers with the recited charge motif and provides a multitude of examples. In addition, the specification shows that polymers as diverse as peptides and polysaccharides, with the specific charge motif show an immunomodulatory effect (See *e.g.*, Example 1, page 49 and Examples 6 and 7, pages 54-55). Furthermore, the specification has incorporated by reference US 5,679,654, US 5,700,787 and WO 00/59515. These documents provide a detailed analysis of polymers, including polysaccharides, with specific charge motifs and their immunomodulatory effects. The teachings in these documents show that polymers with the motif recited in the instant application have a predictable and consistent immunomodulatory effect, while polymers with a slightly different charge motif do not have such an effect (See *e.g.*, WO 00/59515, pages 35-43). Thus, the speciation provides a representative number of species of the claimed genus.

According to the Examiner, "the term "comprising" is open language that opens the claimed polymers to include additional molecules wherein the methods are not the result of the charge motif of the polymers at all". Respectfully, as demonstrated under the enablement rejection, Applicant

maintains that the Examiner's interpretation of claims reciting the connector "comprising" has no legal basis.

Thus, Applicant has provided a representative number of species for the claimed genus, and Applicant has shown that correlation exists between the structure of the recited polymers and the function of the claimed methods of treatment. Based on the teachings in the specification, a person of ordinary skill in the art would understand that Applicant had possession of the claimed invention at the time of filing of the application. In addition, Applicant believes that the Examiner has not shown that Applicant did not have possession of the claimed invention at the time of filing.

Claim Rejections under 35 U.S.C. §103

Claims 1-2, 4-7 and 18 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over WO 00/59515 in view of Tang et al. (2001) *J. Immunol.* 166:1471-1481. According to the Examiner, WO 00/59515 teaches treating Th1 responsive disorders. Also, according to the Examiner, column 23, line 60 to column 24, line 7 of WO 00/59515 teaches that driving the immune response toward a Th1 response when it is desirable to have a Th1 cytokine response to treat disease, as is the case for allergies. Further, according to the Examiner, Tang et al. teaches that allergic inflammation is a Th2-mediated disease and that an immune switch to Th1 can protect Th2-mediated allergic responses.

Applicant respectfully traverses. The combination of the teachings of WO/59515 and Tang et al. does not render obvious the treatment of allergic disorders by administering polymers with the recited charge motif.

Applicant maintains that WO 00/59515 does not teach "switching the immune response from a Th2 response to a Th1 response by the administration of the recited polysaccharides". WO 00/59515 merely teaches that the administration of the recited polysaccharides results in the induction of a Th1 profile. The attempts by the Examiner to equate a switch from a Th2 response to a Th1 response with the induction of a Th1 response are unfounded based on the cited references and the art in general.

The Examiner states on page 16 of the Office Action that "one of ordinary skill in the art *knows* that Th1 responsive disorders are those that "respond" by making the Th cytokine profile

Th1. If the disorder "responds" by making it Th1, then it is not currently Th1. Therefore, it must necessarily be Th2". Respectfully, Applicant disagrees with this reasoning. Firstly, the Examiner's argument is based on what one of skilled in the art allegedly *knows* without providing support for this assertion. Secondly, a disorder that does not results in the induction of a Th1cytokine profile, is merely a disorder that does not result in the induction of a Th1 response. A disorder that fails to respond with a Th1 cytokine profile does not make the disorder a Th2 disorder. For instance, as shown by Tang et al., dendritic cells are responsible for the induction of a Th2, while antigen-presenting macrophages are responsible for the induction of Th1. While the induction of antigen-presenting macrophages would result in the induction of a Th1 response, the induction of a Th1 response does not automatically mean that a Th2 response is not induced, as this would rely on the induction of different cells. Thus, the induction of Th1 and Th2 responses are not necessarily correlated and the induction of a Th1 response does not necessarily imply a switch from Th2 to Th1.

The Examiner further supports the assertion that WO 00/59515 teaches switching the immune response from a Th2 response to a Th1 response by referring to the post-filing teachings of Mazmanian et al. Applicant respectfully disagrees with this reasoning. Mazmanian et al. is a post-filing teaching co-authored by an inventor of the instant application. Thus, Mazmanian et al. cannot be used to support the argument that the instant application was obvious.

Thus, at least for the reasons presented above, the combination of WO00/59515 and Tang et al. does not render obvious the methods of the rejected claims.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 1-7 and 18 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over U.S. Patent 7,026,285 in view of Tang et al. (*supra*). Applicant respectfully requests reconsideration. The cited patent is the U.S. equivalent of WO 00/59515. The rejection should be withdrawn for the same reasons as discussed above in connection with WO 00/59515.

Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 1-7 and 18 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 7,026,285 in view of Tang et al.

CONCLUSION

In view of the foregoing, the present application is believed to be in condition for allowance. A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the application in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, any necessary extension of time is hereby requested. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. B0801.70280US01.

Dated: May 26, 2009

Respectfully submitted,

By: /Erik J. Spek/
Erik J. Spek, Ph.D.
Registration No.: 61,065
WOLF, GREENFIELD & SACKS, P.C.
Federal Reserve Plaza
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
617.646.8000